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ORIGINAL ARTICLE

Brain intrinsic network connectivity in individuals with frequent tanning behavior

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ABSTRACT

Background: Emergent studies suggest a bidirectional relationship between brain functioning and the skin. This neurocutaneous connection may be responsible for the reward response to tanning and, thus, may contribute to excessive tanning behavior. To date, however, this association has not yet been examined. *Objectives*: To explore whether intrinsic brain functional connectivity within the default mode network (DMN) is related to indoor tanning behavior. *Methods*: Resting state functional connectivity (rsFC) was obtained in twenty adults (16 females) with a history of indoor tanning. Using a seed-based [(posterior cingulate cortex (PCC)] approach, the relationship between tanning severity and FC strength was assessed. Tanning severity was measured with symptom count from the Structured Clinical Interview for Tanning Abuse and Dependence (SITAD) and tanning intensity (lifetime indoor tanning episodes/years tanning). *Results*: rsFC strength between the PCC and other DMN regions (left globus pallidus, left medial frontal gyrus, left superior frontal gyrus) is positively correlated with tanning symptom count. rsFC strength between the PCC and salience network regions (right anterior cingulate cortex, left inferior parietal lobe, left inferior temporal gyrus) is correlated with tanning intensity. *Conclusion*: Greater connectivity between tanning severity and DMN and salience network connectivity suggests that heightened self-awareness of salient stimuli may be a mechanism that underlies frequent tanning behavior. These findings add to the growing evidence of brain-skin connection and reflect dysregulation in the reward processing networks in those with frequent tanning.

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Striatum; resting state functional connectivity; reward; tanning; ultraviolet radiation; posterior cingulate cortex

Introduction

Evidence suggests a brain-skin connection whereby a bidirectional relationship exists between neurobiological and psychological factors and the skin. The concept of the skin as the "diffuse brain" was first introduced in 1980 based on the release of peptide hormones from endocrine cells in the skin (1). These hormones influence mood and psychiatric conditions (2). The neurocutaneous connection hypothesis has been shown in those with psoriasis through repeated evidence of the link between psoriasis and personality traits, depression and anxiety that is mediated by hormones generated by the skin (3). Thus, behaviors that affect the skin, such as tanning, may have direct neural inputs from the skin.

Extensive literature has tied the use of tanning beds with increased rates of skin cancer (4,5). Nevertheless, more than 30 million Americans visit tanning beds each year despite known risks mirrors patterns of drug abuse (6). Because frequent tanners demonstrate a reward response after tanning (7), problematic tanning behavior has been compared to other rewarding behavioral disorders like gambling and internet gaming disorders: Harrington et al. (8) showed that 42% of frequent (>3x/week) tanners demonstrated symptoms of "tanning use disorder" as modeled after the Diagnostic and Statistical Manual for Psychiatric Disorders substance abuse and dependence structured clinical interview (e.g. "have you continued tanning despite adverse health effects from tanning?) (8). Hillhouse et al. has operationalized the behavior of continued tanning despite negative consequences using the Structured Interview for Tanning Abuse and Dependence (SITAD) (9) based on the DSM-

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IV Axis 1 Disorders. Thus, there is an emergent evidence suggesting that frequent tanning may share phenomenological and pathophysiological similarities with other reward-related disorders.

Individuals who frequently tan report feelings of reward after tanning attributed to both the desired physical outcomes as well as from the ultraviolet radiation (UVR) (10). When given a choice between a UV-emitting light and a sham light, the majority of frequent tanners choose the UV option and report improved mood afterward (11). Kaur et al (12) proposed that this pleasurable response to tanning occurs through UV activation of pathways involving opioid receptors. In a double-blind study, Kaur et al. reported that the blockade of opioid receptors by naltrexone in frequent tanners reduced preference for UV-emitting tanning beds compared to tanning beds in which UVR was blocked (12). This rewarding effect following UV radiation may be the pathophysiological mechanism driving frequent tanning, a mechanism that mirrors the physiological changes seen in substance use disorder. A previous study examining brain activity during real and sham-UVR found that real, but not sham, UVR was associated with greater cerebral blood flow (as measured by single photon emission tomography) in the left caudate, right putamen and anterior insula (13). Our group also recently showed that dopamine efflux from the left caudate was greater after administration of UVR in individuals endorsing symptoms of tanning addiction. The observed increase in UVR-induced dopamine efflux correlated with tanning intensity (measured as number of lifetime indoor tanning uses divided by years of tanning), indicating an association between greater reward response to UVR with greater intensity of tanning bed use (7).

The goal of this study was to expand upon the sparse, but relevant literature regarding tanning as a reward-related disorder, by investigating brain functional connectivity as it relates to frequent tanning. Resting state functional connectivity (rsFC) examines spontaneous fluctuations in fMRI blood oxygen level dependent (BOLD) signal when an individual is not engaged in any specific task (14). rsFC studies have identified consistent synchronous activations between brain regions at rest that are referred to as resting state networks (RSNs). The primary RSN is the default mode network (DMN), which comprises the precuneus/posterior cingulate cortex (PCC), the medial prefrontal cortex (MPFC), the lateral and medial temporal cortex, and the inferior parietal lobe/angular gyrus (IPL/AG). These regions are functionally connected at rest (15,16). The DMN operates independently of task-related activity and is especially active during self-reflection. Studies of rsFC have shown stronger connectivity between self-monitoring and reward brain regions in addicted populations (17,18), and alterations in rsFC have been shown in reward-related disorders (19) including substances of abuse (20–22), and non-substance reward disorders, e.g. internet gaming addiction (23–25). Specifically, the strength of DMN connectivity has been shown in components underlying these reward disorders including response inhibition, negative affect, and reward (26). While the literature addressing the neural underpinnings of problematic tanning behavior is sparse, it is likely that there is a similar link between self-monitoring and reward in these individuals.

The PCC is a primary hub in the DMN (14,27) and is involved in self-relevant thoughts and perception of the external environment (17,28). In a review of PCC function, Pearson et al. (29) concluded that self-relevant thoughts, particularly in the context of awareness of external circumstances, have been linked to reward-prediction and behavior, as external cues prompt reward-seeking behavior (29). Processing of self-relevant stimuli has been shown to be altered in the case of frequent reward-seeking behavior, especially after the presentation of external, reward-relevant cues (30,31). In this study, we examined the relationship between functional brain connectivity in participants with a range of indoor tanning frequencies and tanning use disorder symptoms. We hypothesized that the PCC, a key node in the DMN, would demonstrate greater rsFC with areas related to valuation of stimuli, which might be related to altered reward processing.

Methods

This study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. Written consent was obtained from all participants, and all data were collected in accordance with the principles outlined in the Declaration of Helsinki.

Participants

Twenty-six participants were recruited through flyers and Internet advertisements to take part in a study assessing the neurological characteristics associated with tanning behavior (7). Participants were Caucasian or Hispanic men and women between 18 and 45- years old, with a Fitzpatrick skin phototype ranging between II and IV (Table 1). Inclusion criteria included a minimum of 10 lifetime indoor tanning episodes, and exclusion criteria included the use of psychoactive medications and fMRI contraindications (e.g. pregnancy, left-handedness, metal in the body). Additionally, participants were excluded if they had any lifetime history of

Table 1. Tanning severity measures correlation with resting state functional connectivity (rsFC) between default mode network (DMN) seed [posterior cingulate cortex (PCC)] and other brain regions.

Cluster Size	X	Y	Z	Brain Region
Tanning symptom count[1]				
119	−18	58	0	L. Medial Frontal Gyrus
110	0	56	30	L. Superior Frontal Gyrus
92	− 6	2	−6	L. Globus Pallidus
Tanning intensity[2]				
199	−48	−66	52	L. Inferior parietal lobule
179	62	−4	−36	R. Inferior Temporal Gyrus
169	6	56	2	R. Anterior Cingulate
167	−62	−18	−14	L. Middle Temporal Gyrus

[1]symptom counts from the Structured Clinical Interview for Tanning Abuse and Dependence (SITAD)
[2]lifetime indoor tanning episodes/years tanning

Diagnostic Statistical Manual (DSM)-IV Substance Dependence, Seasonal Affective, or Body Dysmorphic Disorder, or any active mood, psychotic or anxiety disorder. Six participants were excluded due to insufficient data after motion correction (see procedure below), leaving a total of 20 participants.

Behavioral measures

We collected participants' responses on the Structured Interview for Tanning Abuse and Dependence (SITAD), which was modeled after the Structured Clinical Interview for DSM-IV Axis 1 Substance Dependence Disorders to quantify the degree to which tanning impacts participants' lives, e.g. "has your indoor tanning caused any physical problems or made physical problems worse?" (9). In accordance with DSM-5 substance use disorder criteria, total number of symptoms was used as a gradient. SITAD symptoms include: (i) continued tanning despite failure to fulfill obligations at work, school, or home, (ii) recurrent use that is hazardous to your health, (iii) recurrent use-related legal problems; continued use despite social problems caused by exacerbated use, (iv) use for longer periods of time or more often than intended; persistent desire or unsuccessful efforts to cut down or control use, (v) a great deal of time spent on activities necessary to tanning, (vi) hobbies given up or reduced due to time spent tanning, (vii) use continued despite psychological problems caused by tanning, (viii) need for increased use, and, (ix) withdrawal symptoms experienced. To quantify tanning use severity, lifetime history of sunbed tanning episodes was obtained using a modified Time Line Follow Back (TLFB) (32). The TLFB uses significant life events as chronological anchor points to accurately recall temporal patterns of tanning episodes. A tanning intensity score (total lifetime indoor bed uses divided by total years of use) was calculated to quantify the intensity of indoor tanning use (7).

Imaging data acquisition

Participants were scanned in a Philips Achieva 3.0T at the Advanced Imaging Research Center at the UT Southwestern Medical Center, using a standard head coil. Each participant underwent a three-dimensional, high-resolution magnetization prepared rapid gradient echo (MPRAGE) T1-weighted sequence (repetition time [TR] = 2200 ms, echo time [TE] = 4.60 ms, flip angle [FA] = 12°). All participants underwent a resting state scan while instructed to hold still and keep their eyes closed. The first six participants underwent a six-minute scan, resulting in 212 dynamics, before the protocol was changed to eight minutes (275 dynamics) for the last 14 participants.

Pre-processing

All pre-processing occurred in AFNI. Pre-processing of the fMRI data included temporal alignment via slice-time correction, spatial correction and alignment via rigid body realignment to correct for head motion, removal of linear trend, a bandpass filter of 0.01–0.1 Hz, and the images were spatially smoothed with a Gaussian kernel with full-width-at-half-maximum (FWHM) of 6 mm. Nuisance regressors for white matter and cerebral spinal fluid time courses were removed. Finally, spatial normalization to an MNI template using Analysis of Functional Neuroimaging software (AFNI) (33).

We implemented motion correction following guidelines by Power et al (34). Each frame collected during the scan was examined for movement >0.5mm from the reference frame. Frames with >0.5 mm movement were removed from the timeseries to attenuate the effect of motion variability on signal (34–36). To ensure sufficient, high-quality data for analysis, and to maintain homogeneity between 6-minute scans and 8-minute scans, we applied a consistent frame threshold for both scan lengths. In line with Power et al. (34), we first determined that using an 85% frame threshold in the 6-minute (shorter duration) scan resulted in 185 frames after scrubbing. We then applied the same 185-frame threshold on the data from the 8-minute scans. This approach maximizes the data by retaining the same number of frames while minimizing any discrepancy in quality between the two scan lengths.

Analysis

All analyses were done in AFNI (33). We used a seed-based rsFC approach using the bilateral PCC as the

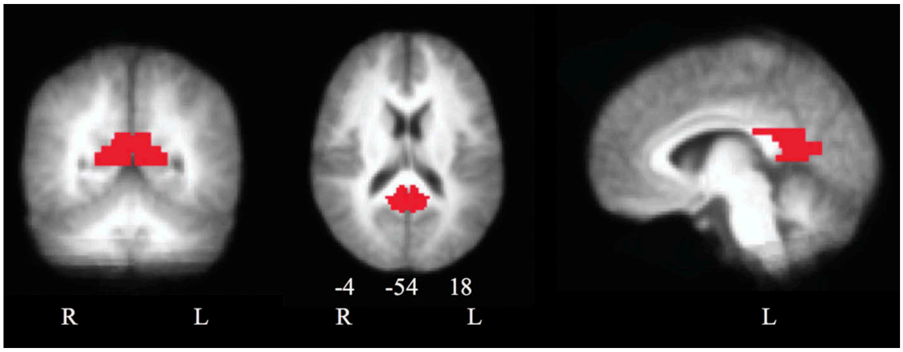

Figure 1. Using the posterior cingulate cortex (PCC) as the seed, tanning symptom count correlated with resting state connectivity strength between the (A) posterior cingulate cortex (PCC)-L medial frontal gyrus, (B) PCC-left superior frontal gyrus, and (C) PCC-left globus pallidus.

seed region given its role within the default mode network. The PCC seed was created using the AAL Atlas (37) (Figure 1).

The cross-correlation coefficients (cc) between the PCC seed and all other voxels in the brain were calculated to generate correlation maps per person. A Fisher z-transformation was performed to convert the correlation maps to z maps for voxel-based analysis (VBA). An average structural MPRAGE anatomical image was created from all participants' structural images (acquired via MPRAGE sequence) and used as an anatomical underlay. We then used the most recent version of 3dClustSim, which calculates the non-Gaussian spatial autocorrelation function, to estimate the probability of false positives based on smoothness of the voxel map and clustering threshold (38,39). This determined that, with a family wise error (FWE) correction at a cluster forming threshold of $p = 0.005$, using our PCC mask (Figure 1), our cluster threshold was 92 voxels. To evaluate the relationships between tanning intensity and rsFC, we then tested correlations between the z scores from the peak voxels within these clusters and scores associated with tanning intensity score and tanning symptom count.

Results

Demographic and clinical information

The final sample of 20 participants (16 female) was 29.7 ± 5.9 (mean±standard deviation) years old with 15.1 ± 1.8 years of education. Fifteen were white and 5 were Hispanic. Participants reported 11.5 ± 6.8 years of tanning (range 1 to 24) and 913.5 ± 986.9 (range 11–3426) lifetime indoor tanning episodes. Tanning symptom count (range 0–8) was 2.4 ± 3.0 and tanning intensity score (range 2–267) was 77.3 ± 74.8.

There was no effect of sex on total lifetime tanning episodes ($t(5) = -0.43$, $p = 0.69$), tanning intensity score ($t(10) = -1.16$, $p = 0.27$), or SITAD score ($t(4) = 0.19$, $p = 0.86$). As expected, there was a correlation between age and total lifetime tanning episodes, $r(18) = 0.68$, $p = 0.0009$, which supported our approach to use tanning intensity score in subsequent analyses. There was no correlation between age and tanning intensity score, $r(18) = 0.22$, $p = 0.3562$.

Correlates of tanning severity and resting state functional connectivity

The number of tanning addiction symptoms (tanning symptom count) significantly correlated with PCC-PFC connectivity, including the left medial frontal gyrus and the left superior frontal gyrus. Symptom count was also correlated with PCC-left ventral anterior cingulate connectivity strength (Table 1, Figure 2).

The tanning intensity score was correlated with PCC-DMN regions functional strength in the left inferior parietal lobule, right inferior temporal gyrus, left middle temporal gyrus, and the right anterior cingulate cortex (BA 32) (Table 1, Figure 3).

Discussion

In this examination of intrinsic brain functional connectivity in indoor tanners, we found a correlation between rsFC and tanning symptom count whereby tanning addiction symptom count was positively correlated with greater rsFC strength between PCC and left globus pallidus, indicating a heightened role of self-relevant and reward processing in the severity of tanning use disorder. Additionally, tanning symptom count correlated with rsFC between PFC and reward-related regions, including the left medial frontal gyrus

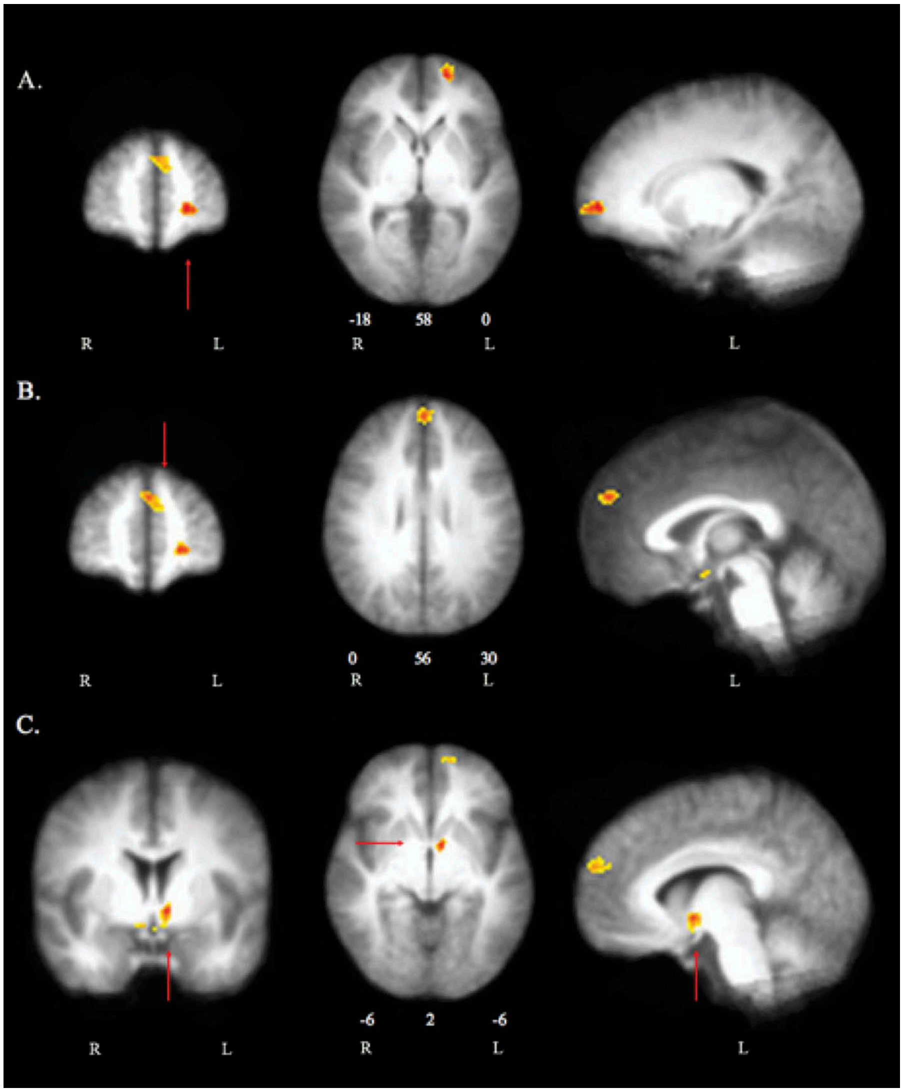

Figure 2. Using the posterior cingulate cortex (PCC) as the seed, tanning intensity score correlated with resting state functional connectivity strength between the (A) posterior cingulate (PCC)-left inferior parietal lobule, (B) PCC-right inferior temporal gyrus, (C) PCC-right anterior cingulate, and (D) PCC-left middle temporal gyrus.

and the left superior frontal gyrus. As nodes within the DMN, these regions play a role in self-relevant processing (27,40–42). The relationship between PCC-medial frontal cortex connectivity and number of tanning addiction symptoms suggest a heightened role of self-relevant processing with greater severity of this disorder. Tanning intensity score was significantly correlated with rsFC in the DMN, including PCC-left inferior parietal lobule, PCC-left middle temporal gyrus, right inferior temporal gyrus, and the anterior portion of the right anterior cingulate.

These DMN regions have been associated with a subset of functions in substance use disorders and behavioral addictions. For example, the inferior parietal lobule was found to be specifically involved in the episodic recollection component of autobiographical thought, which may contribute to the role of memory in addiction (43,44). The middle temporal gyrus has been reported to show greater activation in response to rewarding cues (e.g. alcohol, cocaine) compared to neutral controls, and, therefore, implicated in reward response (45,46). Last, the inferior temporal gyrus has been linked with impulsivity in those with internet gaming addiction (47). Together, stronger connectivity between default mode network and self-relevant processing networks, in conjunction with measures of tanning severity, are consistent with the literature of other addiction disorders (17).

The DMN interacts with the salience network (SN), which comprises the medial prefrontal cortex and the anterior cingulate cortex, to attribute valuation to stimuli in nicotine users (18,48). Janes et al. (49)

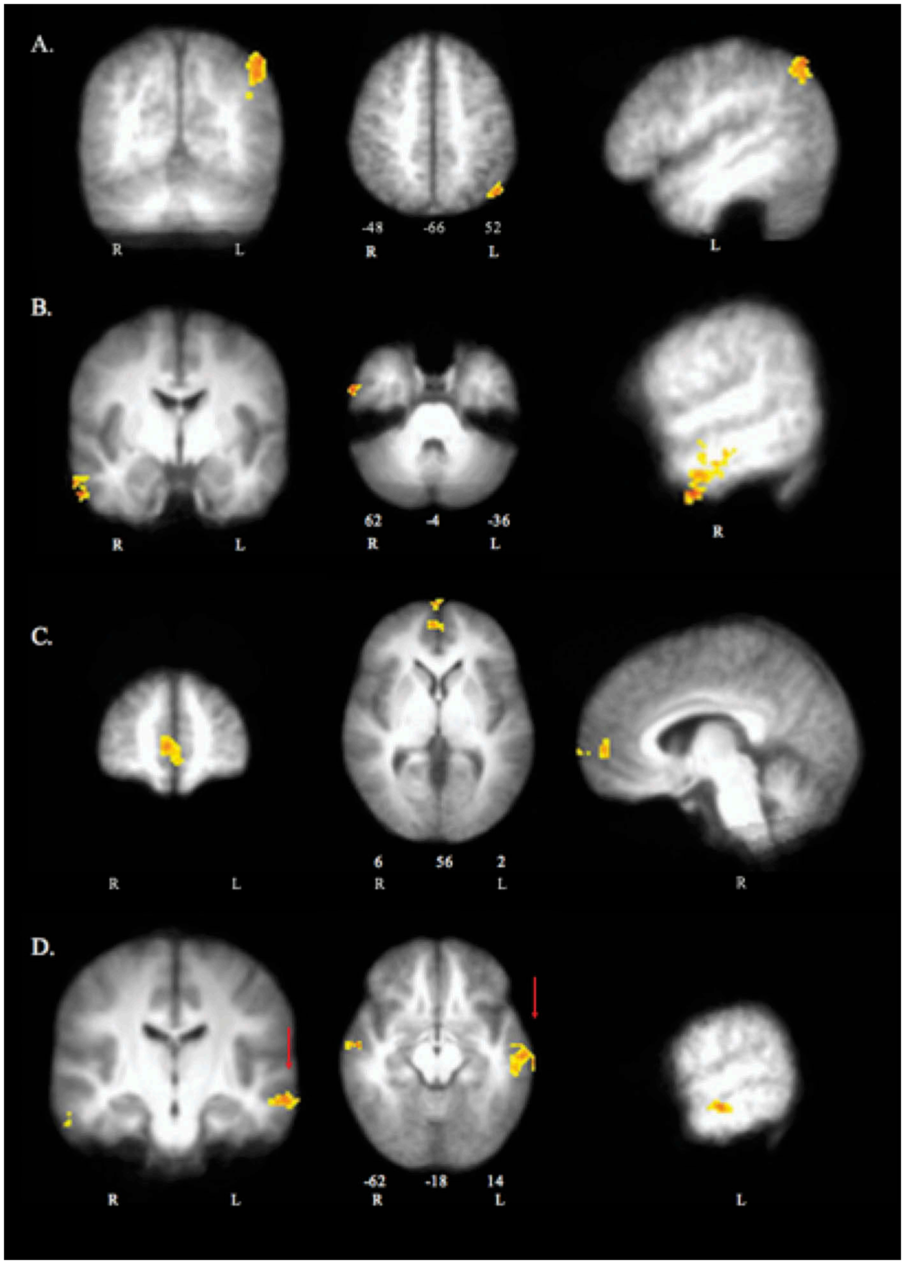

Figure 3. Tanning Intensity Score correlates with (A) posterior cingulate (PCC)-left inferior parietal lobule functional connectivity, (B) PCC-right inferior temporal gyrus functional connectivity, (C) PCC-right anterior cingulate functional connectivity, and (D) PCC-left middle temporal gyrus functional connectivity.

demonstrated that the DMN was less suppressed in nicotine users viewing smoking cues (relative to neutral cues) and that this diminished inhibition was related to reactivity to cues in SN. Thus, the activation of the salience network may be related to suppressed inhibition of the DMN, which may play a role in drug use (18,49).

Number of tanning symptoms also positively correlated with rsFC in PCC-left globus pallidus. The globus pallidus is part of the SN, directly signals the substantia nigra, and is involved in the encoding of reward (50). Thus, a positive correlation between symptoms of tanning use disorder and DMN-SN connectivity suggests that the salience of self-relevant stimuli may be more relevant in individuals with tanning use disorder.

Because these SN and DMN regions are involved in self-monitoring and reward, greater self-monitoring in relation to reward may be related to the intensity of tanning addiction. This might be the case because hyper-vigilant monitoring of the relevance of external stimuli to the self may facilitate reward acquisition. The awareness of external cues (exteroception) is closely linked with motivation and reward since the pursuit of natural rewards (e.g. acquisition of food) is necessary for survival. The function of the PCC and precuneus, which together comprise the posterior node of the DMN, has been most closely associated with exteroception, and individuals with substance use disorders show greater activity in the PCC during tasks of self-relevance. Alterations in PCC connectivity have been implicated across several substance and behavioral addictions. In marijuana users, PCC-anterior cingulate connectivity is greater during the presentation of marijuana cues than natural cues (51). In nicotine users, PCC activity correlates with number of Fagerstrom Test for Nicotine Dependence (FTND) symptoms during nicotine cue presentation (52). Similarly, activity before unsuccessful response inhibition in the posterior cingulate has been correlated with alcohol use disorder severity (53). Similar findings have also been seen in individuals with cocaine use disorder, who demonstrate greater precuneus activity when viewing cocaine cues compared to neutral cues (54). In light of these studies, greater PCC-DMN connectivity suggests that heightened self-referential processing may play a role in tanning addiction severity. In line with other studies of addiction disorders, this greater valuation of self-relevant stimuli may occur at the cost of other cognitive processes (e.g. executive control). Additionally, greater connectivity with the anterior cingulate indicates heightened error monitoring in conjunction with self-relevant thoughts (48). Together, these results may indicate that cues relevant to the self (as opposed to other, long-term goals) may be internally valued more than the potentially negative effects associated with abstinence. In individuals with tanning use disorder, this could suggest that the rewards of tanning are valued more highly than skin cancer prevention (18).

Limitations

Interpretation of these findings is limited by our relatively small sample size (N = 20), and thus, these results should be corroborated in a larger sample. As these data are cross-sectional, the cause/effect directionality of these results cannot be determined. In line with current work examining sex differences and the effect of the hormonal milieu on brain function, future work should include the effect of menstrual cycle day on these findings. However, analyses for sex differences in this sample revealed none. A longer average scan time may additionally benefit these results, and the motion correction method used in this study is not the only approach to motion correction. While this method comprises excision of contaminated data frames, other methods opt for detection and removal of artefactual signal within a frame. While both approaches have advantages, this method has been shown repeatedly to improve the unwanted effects of subject motion (34–36). This method, in conjunction with the traditional band-pass filter applied during preprocessing, has strong support for being the most effective method of artifact removal. While a scan time of 6 minutes is short, and the scrubbing procedure further reduces the total number of frames to 185 per subject, our final number of frames after scrubbing is similar to but more conservative than the threshold originally determined by Power et al. (34).

Additionally, these results could be examined with rsFC patterns in non-tanning controls. However, our findings of connectivity strength correlation with symptom count and indoor tanning episodes would not be possible in a sample of never-tanners. Thus, in this study, we encompass the broad population of users by including individuals with lesser and greater amounts of use (tanning) and by using a continuous spectrum of SITAD scores, ranging from no tanning use disorder (0–2) symptoms to severe tanning use disorder (8 symptoms).

Conclusions

These findings support the literature regarding the neurocutaneous mechanism of reward associated with tanning. The findings demonstrate a linear, positive relationship between tanning severity and rsFC strength between brain regions involved in exteroception and salience. This relationship suggests that rsFC underlying sensitivity to external, self-relevant stimuli is associated with greater severity of tanning use. Attribution of salience to self-relevant cues is a key feature in compulsive disorders, and the present work suggests that it may be a component of tanning use disorder as well.

Author Contributions

AK wrote the initial draft. FF and BA provided primary input on the draft, with assistance from JPS, PMA, and JS. AK performed all analyses with oversight from FF. BA designed the study with assistance from JPS, PMA, and JLP and was responsible for oversight of recruitment, assessment, and assessment. JLP and PMA had primarily responsibility of participant screening and assessment.

Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of UT Southwestern Medical center and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Disclosures

The authors declare no conflicts of interest.

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References

1. Pearse AGE. The neuroendocrine (APUD) cells of the skin. Am J Dermatopathol. [Internet]. 1980 [accessed 2016 Dec 23]. 2(2):121–23. http://journals.lww.com/amjdermatopathology/Fulltext/1980/00220/The_neuroendocrine__APUD__cells_of_the_skin_.2.aspx
2. Urpe M, Buggiani G, Lotti T. Stress and psychoneuroimmunologic factors in dermatology. Dermatol Clin. 2005 Oct;23(4):609–17.
3. Chapman BP, Moynihan J. The brain–skin connection: role of psychosocial factors and neuropeptides in psoriasis. Expert Rev Clin Immunol. 2009 Nov;5(6):623–27. doi:10.1586/eci.09.56.
4. Colantonio S, Bracken MB, Beecker J. The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. J Am Acad Dermatol. 2014 May;70(5):847–57.e18. doi:10.1016/j.jaad.2013.11.050.
5. Mosher CE, Danoff-Burg S. Addiction to indoor tanning: relation to anxiety, depression, and substance use. Arch Dermatol. 2010 Apr 1;146(4):412–17. doi:10.1001/archdermatol.2009.385.
6. Heckman CJ, Darlow SD, Kloss JD, Munshi T, Manne SL. Contextual factors, indoor tanning, and tanning dependence in young women. Am J Health Behav. 2015 May 1;39(3):372–79. doi:10.5993/AJHB.39.3.10.
7. Aubert PM, Seibyl JP, Price JL, Harris TS, Filbey FM, Jacobe H, Devous MD, Adinoff B. Dopamine efflux in response to ultraviolet radiation in addicted sunbed users. Psych Res. 2016 Apr;7(251):7–14. doi:10.1016/j.pscychresns.2016.04.001.
8. Harrington CR, Beswick TC, Leitenberger J, Minhajuddin A, Jacobe HT, Adinoff B. Addictive-like behaviours to ultraviolet light among frequent indoor tanners: addictive-like behaviours among indoor tanners. Clin Exp Dermatol. 2011 Jan;36(1):33–38. doi:10.1111/j.1365-2230.2010.03882.x.
9. Hillhouse JJ, Baker MK, Turrisi R, Shields A, Stapleton J, Jain S, Longacre I. Evaluating a measure of tanning abuse and dependence. Arch Dermatol. 2012 Jul 1;148(7):815. doi:10.1001/archdermatol.2011.2929.
10. Kourosh AS, Harrington CR, Adinoff B. Tanning as a behavioral addiction. Am J Drug Alcohol Abuse. 2010 Aug;36(5):284–90. doi:10.3109/00952990.2010.491883.
11. Feldman SR, Liguori A, Kucenic M, Rapp SR, Fleischer AB, Lang W, Kaur M. Ultraviolet exposure is a reinforcing stimulus in frequent indoor tanners. J Am Acad Dermatol. 2004 Jul;51(1):45–51. doi:10.1016/j.jaad.2004.01.053.
12. Kaur M, Liguori A, Lang W, Rapp SR, Fleischer AB, Feldman SR. Induction of withdrawal-like symptoms in a small randomized, controlled trial of opioid blockade in frequent tanners. J Am Acad Dermatol. 2006 Apr;54(4):709–11. doi:10.1016/j.jaad.2005.11.1059.
13. Harrington CR, Beswick TC, Graves M, Jacobe HT, Harris TS, Kourosh S, Devous MD, Adinoff B. Activation of the mesostriatal reward pathway with exposure to ultraviolet radiation (UVR) vs. sham UVR in frequent tanners: a pilot study: mesostriatal activation in frequent tanners. Addict Biol. 2012 May;17(3):680–86. doi:10.1111/adb.2012.17.issue-3.
14. Fox MD. Clinical applications of resting state functional connectivity. Front Syst Neurosci. [Internet]. 2010 [accessed 2016 Feb 29]. http://journal.frontiersin.org/article/10.3389/fnsys.2010.00019/abstract.
15. Horn A, Ostwald D, Reisert M, Blankenburg F. The structural–functional connectome and the default mode network of the human brain. NeuroImage. 2014 Nov 15;102(Part 1):142–51. doi:10.1016/j.neuroimage.2013.09.069.
16. Chen S, Ross TJ, Zhan W, Myers CS, Chuang K-S, Heishman SJ, Stein EA, Yang Y. Group independent component analysis reveals consistent resting-state networks across multiple sessions. Brain Res. 2008 Nov;1239:141–51. doi:10.1016/j.brainres.2008.08.028.
17. DeWitt SJ, Ketcherside A, McQueeny TM, Dunlop JP, Filbey FM. The hyper-sentient addict: an exteroception model of addiction. Am J Drug Alcohol Abuse. 2015 Sep 3;41(5):374–81. doi:10.3109/00952990.2015.1049701.
18. Sutherland MT, McHugh MJ, Pariyadath V, Stein EA. Resting state functional connectivity in addiction: lessons learned and a road ahead. NeuroImage. 2012 Oct;62(4):2281–95. doi:10.1016/j.neuroimage.2012.01.117.
19. Moeller SJ, Paulus MP. Toward biomarkers of the addicted human brain: using neuroimaging to predict relapse and sustained abstinence in substance use disorder. Prog Neuropsychopharmacol Biol Psych. 2018 Jan;80:143–54. doi:10.1016/j.pnpbp.2017.03.003.
20. Kelly C, Zuo X-N, Gotimer K, Cox CL, Lynch L, Brock D, Imperati D, Garavan H, Rotrosen J, Castellanos FX, et al. Reduced interhemispheric resting state functional connectivity in cocaine addiction. Biol Psych. 2011 Apr 1;69(7):684–92. doi:10.1016/j.biopsych.2010.11.022.
21. Hong LE, Gu H, Yang Y, Ross TJ, Salmeron BJ, Buchholz B, Thaker GK, Stein EA. Association of nicotine addiction and nicotine's actions with separate cingulate cortex functional circuits. Arch Gen Psych. 2009 Apr;66(4):431–41. doi:10.1001/archgenpsychiatry.2009.2.
22. Liao Y, Tang J, Fornito A, Liu T, Chen X, Chen H, Xiang X, Wang X, Hao W. Alterations in regional homogeneity of resting-state brain activity in ketamine

addicts. Neurosci Lett. 2012 Jul 26;522(1):36–40. doi:10.1016/j.neulet.2012.06.009.
23. Ding W, Sun J, Sun Y, Zhou Y, Li L, Xu J, Du Y-S, Hampson M. Altered default network resting-state functional connectivity in adolescents with internet gaming addiction. Hampson M, Editor. PLoS ONE. 2013 Mar 26;8(3):e59902. doi:10.1371/journal.pone.0059902.
24. Wee C-Y, Zhao Z, Yap P-T, Wu G, Shi F, Price T, Du Y, Xu J, Zhou Y, Shen D, et al. Disrupted brain functional network in internet addiction disorder: a resting-state functional magnetic resonance imaging study. Plos One. 2014 Sep 16;9(9):e107306. doi:10.1371/journal.pone.0107306.
25. Cilia R, Cho SS, van Eimeren T, Marotta G, Siri C, Ko JH, Pellecchia G, Pezzoli G, Antonini A, Strafella AP. Pathological gambling in patients with Parkinson's disease is associated with fronto-striatal disconnection: A path modeling analysis. Mov Disord. 2011 Feb 1;26 (2):225–33. doi:10.1002/mds.23480.
26. Vaidya CJ, Gordon EM. Phenotypic variability in resting-state functional connectivity: current status. Brain Connect. 2013 Apr;3(2):99–120. doi:10.1089/brain.2012.0110.
27. Greicius MD, Krasnow B, Reiss AL, Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proc Natl Acad Sci. 2003;100 (1):253–58. doi:10.1073/pnas.0135058100.
28. Fransson P, Marrelec G. The precuneus/posterior cingulate cortex plays a pivotal role in the default mode network: evidence from a partial correlation network analysis. NeuroImage. 2008 Sep;42(3):1178–84. doi:10.1016/j.neuroimage.2008.05.059.
29. Pearson JM, Heilbronner SR, Barack DL, Hayden BY, Platt ML. Posterior cingulate cortex: adapting behavior to a changing world. Trends Cogn Sci. 2011 Apr;15 (4):143–51. doi:10.1016/j.tics.2011.02.002.
30. Filbey FM, Schacht JP, Myers US, Chavez RS, Hutchison KE. Marijuana craving in the brain. Proc Natl Acad Sci. 2009;106(31):13016–21. doi:10.1073/pnas.0903863106.
31. Goldstein RZ, Craig AD (Bud), Bechara A, Garavan H, Childress AR, Paulus MP, Volkow ND. The neurocircuitry of impaired insight in drug addiction. Trends Cogn Sci. 2009 Sep;13(9):372–80. doi:10.1016/j.tics.2009.06.004.
32. Fals-Stewart W, O'Farrell TJ, Freitas TT, McFarlin SK, Rutigliano P. The timeline followback reports of psychoactive substance use by drug-abusing patients: psychometric properties. J Consult Clin Psychol. 2000 Feb;68(1):134–44. doi:10.1037/0022-006X.68.1.134.
33. Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res. 1996;29:162–73. doi:10.1006/cbmr.1996.0014.
34. Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. NeuroImage. 2012 Feb;59(3):2142–54. doi:10.1016/j.neuroimage.2011.10.018.
35. Power JD, Schlaggar BL, Petersen SE. Recent progress and outstanding issues in motion correction in resting state fMRI. NeuroImage. 2015 Jan;15:536–51. doi:10.1016/j.neuroimage.2014.10.044.
36. Power JD, Mitra A, Laumann TO, Snyder AZ, Schlaggar BL, Petersen SE. Methods to detect, characterize, and remove motion artifact in resting state fMRI. NeuroImage. [Internet]. 2014 Jan [accessed 2017 Dec 7]; 84:320–41. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3849338/
37. Jung WH, Jang JH, Park JW, Kim E, Goo E-H, Im O-S, Kwon JS, Margulies D. Unravelling the intrinsic functional organization of the human striatum: a parcellation and connectivity study based on resting-state fMRI. Margulies D, editor. PLoS ONE. 2014 Sep 9;9(9): e106768. doi:10.1371/journal.pone.0106768.
38. Cox RW, Chen G, Glen DR, Reynolds RC, Taylor PA FMRI clustering in AFNI: false positive rates redux. ArXiv170204845 Q-Bio Stat [Internet]. 2017 Feb 15 [accessed 2017 Apr 27]. http://arxiv.org/abs/1702.04845.
39. Eklund A, Nichols TE, Knutsson H. Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. Proc Natl Acad Sci. 2016 Jul 12;113 (28):7900–05. doi:10.1073/pnas.1602413113.
40. Damoiseaux JS, Rombouts S, Barkhof F, Scheltens P, Stam CJ, Smith SM, Beckman CF. Consistent resting-state networks across healthy subjects. Proc Natl Acad Sci. 2006; 103(37):13848–53. doi:10.1073/pnas.0601417103.
41. De Luca M, Beckmann CF, De Stefano N, Matthews PM, Smith SM. fMRI resting state networks define distinct modes of long-distance interactions in the human brain. NeuroImage. 2006 Feb;29(4):1359–67. doi:10.1016/j.neuroimage.2005.08.035.
42. Gusnard DA, Akbudak E, Shulman GL, Raichle ME. Medial prefrontal cortex and self referential mental activity: relation to a default moe of brain function. Pnas. 2001;98(7):4259–64. doi:10.1073/pnas.071043098.
43. Andrews-Hanna JR, Saxe R, Yarkoni T. Contributions of episodic retrieval and mentalizing to autobiographical thought: evidence from functional neuroimaging, resting-state connectivity, and fMRI meta-analyses. NeuroImage. 2014 May;91:324–35. doi:10.1016/j.neuroimage.2014.01.032.
44. Hyman SE, Malenka RC, Nestler EJ. Neural mechanisms of addiction: the role of reward-related learning and memory. Annu Rev Neurosci. 2006;29:565–98. doi:10.1146/annurev.neuro.29.051605.113009.
45. Vollstädt-Klein S, Wichert S, Rabinstein J, Bühler M, Klein O, Ende G, Hermann D, Mann K. Initial, habitual and compulsive alcohol use is characterized by a shift of cue processing from ventral to dorsal striatum: striatal activation in compulsive drinking. Addiction. 2010 Oct;105 (10):1741–49. doi:10.1111/j.1360-0443.2010.03022.x.
46. Wexler BE, Gottschalk CH, Fulbright RK, Prohovnik I, Lacadie CM, Rounsaville BJ, Gore JC. Functional magnetic resonance imaging of cocaine craving. Am J Psych. 2001;158(1):86–95. doi:10.1176/appi.ajp.158.1.86.
47. Ding W, Sun J, Sun Y, Chen X, Zhou Y, Zhuang Z, Li L, Zhang Y, Xu J-R, Du Y-S. Trait impulsivity and impaired prefrontal impulse inhibition function in adolescents with internet gaming addiction revealed by a Go/No-Go fMRI study. Behav Brain Funct. 2014;10(1):1. doi:10.1186/1744-9081-10-20.
48. Carter CS, van Veen V. Anterior cingulate cortex and conflict detection: an update of theory and data.

Cogn Affect Behav Neurosci. 2007 Dec;7(4):367–79. doi:10.3758/CABN.7.4.367.
49. Janes AC, Betts J, Jensen JE, Lukas SE. Dorsal anterior cingulate glutamate is associated with engagement of the default mode network during exposure to smoking cues. Drug Alcohol Depend. 2016 Oct;167:75–81. doi:10.1016/j.drugalcdep.2016.07.021.
50. Rossi JP, Peden C, Castellanos O, Foote KD, Gunduz A, Okun MS. The human subthalamic nucleus and globus pallidus internus differentially encode reward during action control. Hum Brain Mapp. [Internet]. 2017 Jan 1 [accessed 2017 Feb 11]; 38:1952–64. http://onlinelibrary.wiley.com/doi/10.1002/hbm.23496/abstract
51. Filbey FM, Dunlop J. Differential reward network functional connectivity in cannabis dependent and non-dependent users. Drug Alcohol Depend. 2014 Jul;140:101–11. doi:10.1016/j.drugalcdep.2014.04.002.
52. Claus ED, Blaine SK, Filbey FM, Mayer AR, Hutchison KE. Association between nicotine dependence severity, BOLD response to smoking cues, and functional connectivity. Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol. 2013 Nov;38(12):2363–72. doi:10.1038/npp.2013.134.
53. Claus ED, Ewing SWF, Filbey FM, Sabbineni A, Hutchison KE. Identifying neurobiological phenotypes associated with alcohol use disorder severity. Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol. 2011 Sep;36(10):2086–96. doi:10.1038/npp.2011.99.
54. Grant S, London ED, Newlin DB, Villemagne VL, Liu X, Contoreggi C, Phillips RL, Kimes AS, Margolin A. Activation of memory circuits during cue-elicited cocaine craving. Proc Natl Acad Sci USA. 1996 Oct 15;93(21):12040–45. doi:10.1073/pnas.93.21.12040.